Endogenous hormones subtly alter women's response to heat stress

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CARPENTER, A. J., AND S. A. NUNNELEY. *Endogenous hormones subtly alter women's response to heat stress.* J. Appl. Physiol. 65(5): 2313–2317, 1988.—The thermoregulatory responses of menstruant women to exercise in dry heat (dry-bulb temperature/wet-bulb temperature = 48/25°C) were evaluated at three times during the menstrual cycle: menstrual flow (MF), 3–5 days during midcycle including ovulation (OV), and in the middle of the luteal phase (LU). Serum concentrations of estradiol-17β (E_2), progesterone (Pg), luteinizing hormone (LH), and follicle-stimulating hormone (FSH) were measured by radioimmunoassay, and these values were used to determine the dates of OV (peak LH and FSH) and LU (peak postovulatory Pg). After heat acclimation, subjects received heat stress tests (HST) consisting of a 2-h cycle-ergometer exercise at 30% of maximal O_2 consumption in the heat. Rectal (T_{re}) and mean skin ($\bar{T}_{sk}$) temperatures, heart rate (HR), and sweat rate on the chest and thigh were recorded continuously. Total sweat loss (M_{sw}), as indicated by weight loss, was recorded every 20 min, and equivalent water replacement was given. Steady-state exercise metabolic rate (M) was measured at 45 and 110 min. Seven of eight subjects had ovulatory cycles during experimental months. At rest, T_{re} was lowest at OV and significantly higher at LU. During steady-state exercise both T_{re} and $\bar{T}_{sk}$ were lowest at OV and significantly higher at LU. There were no differences between phases in M_{sw}, sweat rate on the chest and thigh or M. Despite higher T_{re} and $\bar{T}_{sk}$ at LU, all subjects were able to complete the 2-h of exercise. We conclude that *1*) the menstrual cycle alters temperature regulation without obvious alterations in sweat output or steady-state metabolic rate, *2*) these changes are so subtle that they easily could be missed if hormonal status is not carefully monitored concomitant with HST, and *3*) the magnitude of the changes are small and do not impair a woman's ability to work in dry heat.

thermoregulation; menstrual cycle; estrogen; progesterone; exercise

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REGULAR CHANGES in women's resting core temperature during the menstrual cycle were reported in the 1930s, when investigators noted that an upward shift of 0.5°F followed ovulation and persisted until the onset of menstruation (10). The mechanisms underlying this phenomenon remain unclear despite extensive studies, and there is continuing disagreement concerning the impact of the temperature shift on thermoregulation during exercise and heat stress. Some authors find no measurable effect of the menstrual cycle on thermoregulatory responses to exercise and/or heat stress (8, 12, 17, 22, 23), whereas others report small but significant increments in body temperatures after ovulation (3, 6, 11, 13, 14, 18, 19, 24).

With the exception of Ref. 12, the investigations cited above all documented the menstrual phase of the subjects either by counting days from the onset of menstrual flow (8, 11, 17, 19, 24) or by following basal body temperature (3, 6, 14, 18, 22, 23). Both of these methods are now recognized as unreliable for timing ovulation (2, 8). This fact, together with interindividual variability in hormone levels, means that past studies may have grouped together heat stress data reflecting different ovarian hormone levels. Because these older studies typically have low numbers of subjects, the misplacement of one or two could readily obscure subtle thermoregulatory effects, and this might explain the apparent inconsistencies in the literature.

Our study was designed to test for possible effects of the normal hormone changes associated with the menstrual cycle on the thermoregulatory responses of women to work in heat. We used measurements of hormone levels to capture three distinct points in the hormone cycle: *1*) menstruation, when all the cyclic hormones are low, *2*) the day of ovulation, when estrogen, follicle-stimulating hormone, and luteinizing hormone are high, and *3*) the midluteal progesterone peak, when estrogen is also high.

METHODS

Subjects were eight women who were fully informed regarding the procedures, gave written consent to participate, and were clinically evaluated to assure that all had normal menstrual cycles lasting 21–35 days. No subject had taken oral contraceptives or other hormonal therapy in the 12 mo preceding the study. Percent body fat was determined by water displacement (1), and maximal aerobic capacity ($\dot{V}O_{2\,max}$) was assessed during treadmill running as previously described (9). The subjects' physical characteristics were as follows: age, 27.3 ± 7.1 (SD) yr; height, 159.5 ± 5.0 cm; weight, 53.8 ± 6.6 kg; percent body fat, 21.5 ± 4.6; $\dot{V}O_{2\,max}$, 39.1 ± 4.0 ml·kg^{-1}·min^{-1}.

Documentation of Cycles

Each subject was studied for three complete menstrual cycles; heat stress testing occurred during the third cycle. Each subject kept a daily record of basal body temperature, morning nude weight, symptoms related to her menstrual cycle, physical activity, and any illness or medications.

Hormone levels were measured three times per week

(Monday, Wednesday, and Friday) during all three cycles and on each day of heat stress testing. The subject reported to the laboratory at 8 A.M; three venous blood samples were drawn without stasis at 30-min intervals, a regimen designed to compensate for the pulsatile secretion of gonadotrophic hormones (25). Aliquots of serum from the three samples were pooled for radioimmunoassay of estradiol-17β (E_2), progesterone (Pg), luteinizing hormone (LH), and follicle-stimulating hormone (FSH). Within-assay variability for duplicate samples was 3.7%, and between-assay variability at 50% binding was 12.7%.

Heat Stress Procedures

After completion of the two base-line cycles, the subjects underwent three to seven heat stress exposures. For each session, the subject dressed in shorts, bikini top, and sports shoes and was instrumented for rectal temperature (T_{re}) and heart rate (HR). She then entered the hot chamber [dry-bulb temperature (T_{db}) = 48°C; wet-bulb temperature (T_{wb}) = 25°C] and pedaled a cycle ergometer for 2 h at 30% of her $\dot{V}O_{2\,max}$. Work was interrupted briefly every 20 min for determination of weight loss, and replacement water was consumed. Metabolic rate was measured at 45 min and 110 min to quantify steady-state heat production. The heat stress exposures continued daily until the subject achieved a steady state during the 2nd h of exposure on 2 consecutive days; the steady state was defined as a change in T_{re} of $\leq$0.1°C and a variation in HR of $<$10 beats/min. Because these subjects were active women and testing was conducted during a Texas summer, some subjects were already heat acclimated. At least three heat stress sessions were conducted with each subject, and no more than seven sessions were necessary to demonstrate acclimation as defined above.

The heat stress test (HST) was essentially the same as the acclimation runs, except that instrumentation was added to measure skin temperature (T_{sk}) at five sites and sweat rate at the chest and thigh. After acclimation the subject underwent the HST on 3–5 days surrounding the predicted date of ovulation, twice during the midluteal phase, and during menstruation. If the schedule produced a gap between HST's, runs were added every other day to maintain heat tolerance.

Physiological Measurements

Temperature. T_{re} was measured from a thermistor inserted 10 cm past the anal sphincter. T_{sk}'s were measured with uncovered thermistors held in place by tension rings strapped to the chest, back, forearm, thigh, and calf. A weighted mean T_{sk} ($\bar{T}_{sk}$) was calculated from the five sites as described by Ramanathan (16).

Heart rate. The electrocardiogram was obtained from leads in the CM_5 placement, and HR was determined from the mean R-R interval.

Sweat rates. Total sweat rate was determined from weight loss (±10 g) corrected for urine output and water intake. Local sweat rates at the chest and thigh were obtained with capsules attached at those sites. Desiccated air was metered through the capsules at 1.5–3 l·min^{-1}, a rate adequate to evaporate all secreted sweat. The vapor pressure of the effluent airstream was measured by resistance hygrometry, and its temperature was measured by colocated thermistor. Local sweat rate was calculated as described by Brengelmann (4).

Metabolic rate. Expired gas was collected in Douglas bags, its volume was measured by dry gas meter, and its composition was determined by mass spectrometry. Metabolic rates were calculated as described by Weir (20).

TABLE 1. *Serum concentrations of measured hormones coincident with heat stress tests*

	E_2, ng/ml	Pg, pg/ml	LH, IU/ml	FSH, IU/ml
Menstrual flow	40.1±7.3	<0.5	9.4±1.7	14.1±2.0
Ovulation	231.4±43.3	<0.5	62.5±8.5	29.9±4.0
Midluteal phase	191.4±32.4	15.7±2.9	5.6±0.9	7.3±0.7

Values are means ± SE; n = 7. E_2, estradiol-17β; Pg, progesterone; LH, luteinizing hormone; FSH, follicle-stimulating hormone.

Analysis of Data

Hormone measurements from each subject's third cycle were used to select the HST's that actually coincided with ovulation (OV), the luteal elevation in Pg (LU), and menstrual flow (MF). Ovulation was defined as the day of peak LH concentration provided that it was followed within 7 days by a sustained rise in Pg concentration; the day of the highest recorded Pg value was used for LU.

One subject failed to meet the hormone criteria for OV during the HST cycle. The data from the seven remaining subjects were analyzed by two-way repeated-measures analysis of variance, with hormone status (OV, LU, and MF) and time within the HST used as factors. Significant F ratios ($P < 0.05$) were followed by comparisons by the use of the Scheffé procedure to identify significant between-phase differences.

RESULTS

Hormone data for the critical HST's appear in Table 1. The patterns are as expected for the three menstrual phases. OV showed elevated levels of LH and E_2, LU showed high Pg, and MF was characterized by low levels of all hormones.

Figure 1 summarizes T_{re} for the HST's. Initial (resting) T_{re} averaged 37.3°C for OV, 37.4°C for MF, and 37.6°C for LU, and all differences were statistically significant. This order (LU > MF > OV) persisted during exercise in the heat, and the elevation of LU over MF and OV remained significant. The MF > OV difference, although consistent, was not statistically significant. $\bar{T}_{sk}$ showed the same hierarchy with phase (Fig. 2). Mean heat production values were 244, 242, and 239 W for MF, OV, and LU, respectively; the differences were not significant.

Hormone status had no significant effect on total sweat loss ($\dot{M}_{sw}$) (Fig. 3) or on local sweating measured at chest and thigh (Fig. 4). Steady-state sweat rates were reached in 18.2 ± 3.1 min for thigh and 26.2 ± 4.7 min

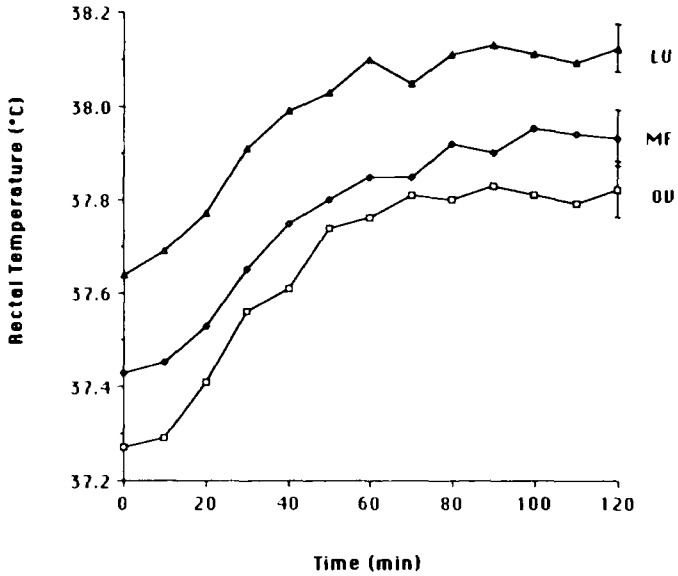

FIG. 1. Rectal temperature as observed in 7 ovulatory women during menstrual flow (MF), ovulation (OV), and midluteal phase (LU). Values are means ± SE; $n = 7$. Exercise started at *time 0*.

for chest. Sweat onset times could not be determined from our data because these acclimated women began to sweat almost immediately on entering the environmental chamber before the sweat capsules were in place.

DISCUSSION

Table 1 shows that the HST data did capture three hormonally distinct points in the menstrual cycle and that the hormone levels were within the expected normal limits. With the MF data as a base line, the midluteal elevation of Pg (Table 1) coincided with significant increases in skin and core temperatures, both at rest and during the HST (Figs. 1 and 2), a finding that agrees with the results of several other heat stress studies (3, 6, 11, 19). This temperature shift is temporally related to the presence of high levels of Pg, which has been shown

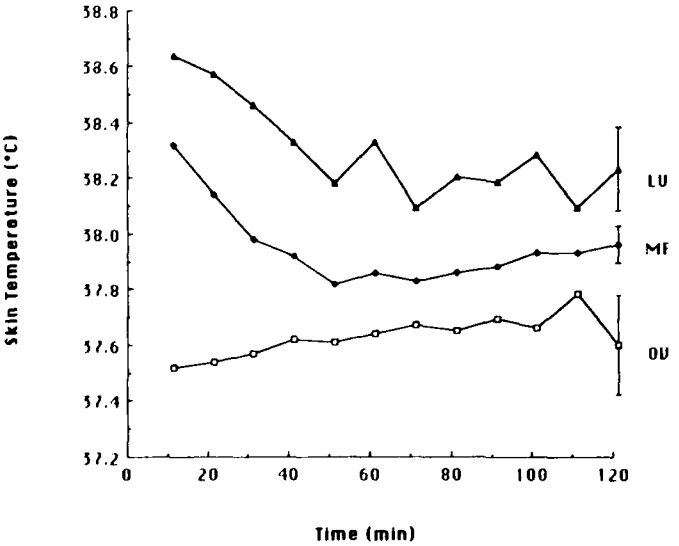

FIG. 2. Mean skin temperature as observed in 7 ovulatory women. See legend of Fig. 1 for definition of abbreviations.

to elevate body temperature (15, 26).

A significant temperature depression below LU occurred at OV in all seven subjects (Figs. 1 and 2). The hormone pattern at OV included high levels of E_2, FSH, and LH (Table 1). Estrogen reportedly depresses temperature in humans (5, 15), but Table 1 shows that E_2 is also present in significant amounts during the midluteal phase with its characteristic temperature rise. The depression of temperature noted at OV never lasted more than 2 consecutive days. This corresponded with the elevation of E_2, LH, and FSH; all three hormones peaked during these 2 days. Considering evidence that E_2 depresses temperature (5, 15), it is possible that the OV temperatures reflect the influence of E_2 unopposed by the pyrogenic effects of Pg. The elevation of temperatures during LU could then be explained as the influence of the high concentration of Pg overcoming the influence of E_2, which was at intermediate concentration during LU (Table 1). Thermal effects of FSH and LH have not been described.

Past studies have emphasized evidence of cycle-related changes in heat dissipation mechanisms, including cutaneous blood flow (19), sweat delay (3, 11, 18, 19), and sweat rate (13, 24). A recent study indicates that there is a change in heat production; direct calorimetry indicates a 10% increase in resting metabolism during LU (21).

The temperature shifts related to the menstrual cycle appear as small offsets that remain constant whether the subject is resting, engaged in light activity, or undergoing heat stress; the normal circadian rhythm remains unchanged (21). A stable alteration of body temperature implies a transient change in the relationship between heat loss and heat gain followed by reestablishment of a balance between the two. Although hormones could theoretically act at either a central controller or the peripheral effectors, the pattern described here is most readily understood as a change to a central controller (6, 14). A mechanism of this type is seen with pyrogens, which act centrally to produce a transient period of heat storage, followed by maintenance of temperature at the new level. Peripheral hormone action would not alter unstressed T_{re} but should affect sweat rate under hot conditions, whereas the reverse was observed in our experiments.

It appears that the menstrual cycle is accompanied by small but real alterations in thermoregulation. LU is dominated by Pg and is characterized by a slight rise in resting metabolism and a stable increase in core temperature; associated alterations in heat stress response (cutaneous perfusion, sweat secretion) may reflect the metabolic and pyrogen-like central actions of the hormone. The slight depression in temperature at ovulation may represent central action of E_2 unopposed by Pg.

The hormone-related temperature differences are of considerable theoretical interest and have created much debate among physiologists over the years, but their practical impact is small. T_{re} shift amounts to <0.5°C (Fig. 1). There is no evidence that menstrual phase has any significant effect on women's tolerance for physical work and heat stress, which is heavily dependent on aerobic fitness, heat acclimation, and individual varia-

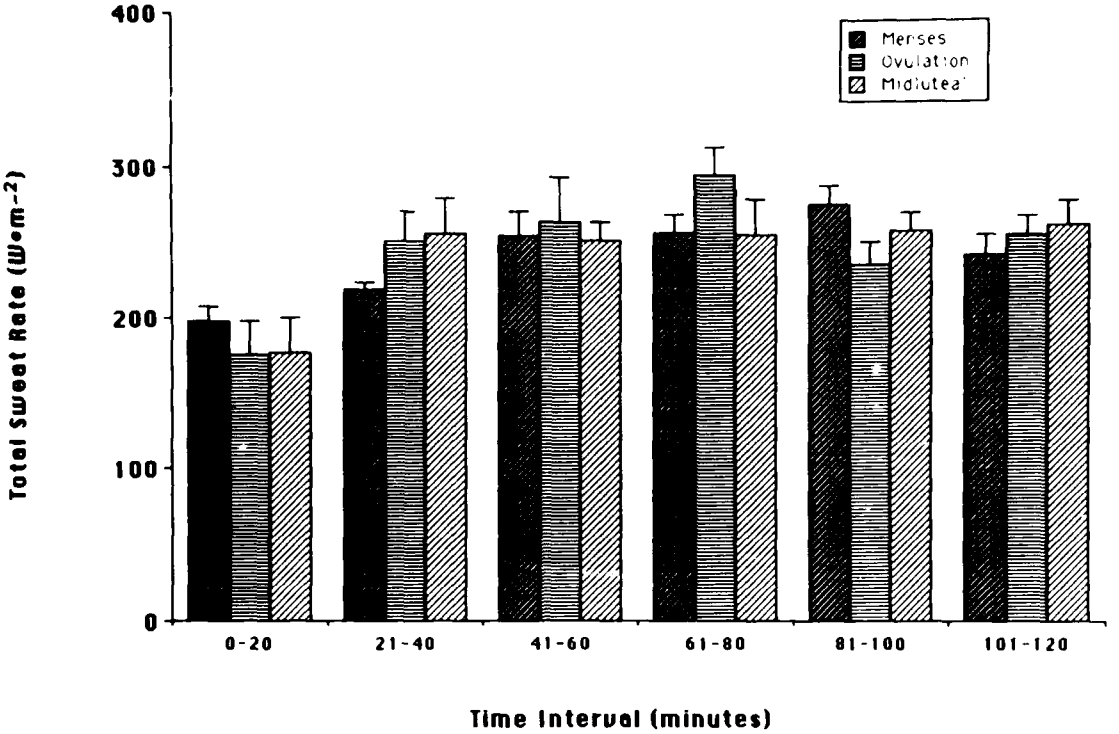

FIG. 3. Total sweating rates as observed in 7 ovulatory women. Values are means ± SE.

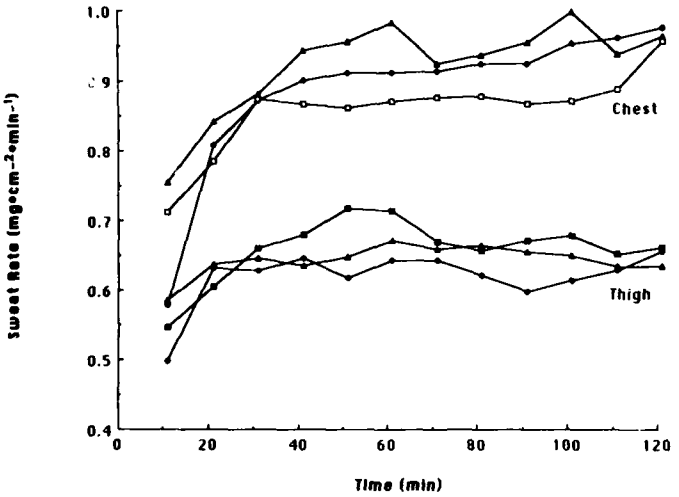

FIG. 4. Local sweating rate as observed in 7 ovulatory women on chest (*top*) and thigh (*bottom*). See legend of Fig. 1 for definition of abbreviations.

tion in heat stress response.

The small amplitude of the cyclic change in body temperature probably explains the variability in the literature on this topic. Without hormone measurements in coordination with heat stress testing, the differences reported here could be missed. Our eighth subject provided an example of this problem. Her HST cycle lasted 35 days (not unusual for her) and appeared clinically normal in all respects; her basal body temperature showed an upward shift near the middle of the cycle. Nevertheless, there was no rise in Pg, and serial HST's showed no temperature change through the cycle. In the absence of hormone measurements, we would have confidently included her data with the others, thus attenuating the finding of the hormone-related shift in stressed temperature.

In summary, the responses of women to exercise and heat stress were studied during three phases of the menstrual cycle: during menses, at ovulation, and during the midluteal peak in Pg concentration. Despite similar sweat evaporation during all heat stress tests, body temperatures were significantly lower at OV and higher during LU. The observed differences were subtle and could easily be missed if hormone levels were not individually documented. The mechanism behind the observed differences in temperature remains to be defined. Temperature changes were not due to changes in sweat production, but differences in sweating threshold may have been a factor. The most likely explanation for these results is a change in set point related to the changing hormonal milieu occurring during the menstrual cycle.

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